Volume 565 July 3, 1989

## SICKLE CELL DISEASE<sup>a</sup>

Editors and Conference Organizers
CHARLES F. WHITTEN and JOHN F. BERTLES

CONTENTS	
Preface. By Charles F. Whitten	xiii
Part I. The Molecular Genetics of Hemoglobin	
The Molecular Genetics of Hemoglobin. By PETER T. CURTIN and YUET WAI KAN	1
Regulatory Regions Flanking the Human Fetal γ-Globin Genes. By Henry J. Lin, David M. Bodine, Tim R. Rutherford, Nicholas P. Anagnou, Kevin T. McDonagh, Timothy J. Ley, and Arthur W. Nienhuis	13
The Emerging Complexity of Genetic Control of Persistent Fetal Hemoglobin Biosynthesis in Adults. By SAMUEL H. BOYER	23
Gene Transfer: A Potential Approach to Gene Therapy for Sickle Cell Disease.  By Arthur Bank, Dina Markowitz, and Norma Lerner	37
Prenatal Diagnosis of Sickle Cell Anemia—1988. By HAIG H. KAZAZIAN, JR., DEBORAH G. PHILLIPS, CAROL E. DOWLING, and CORINNE D. BOEHM	44
Prenatal Diagnosis for Sickle Cell Disease: A Survey of the United States and Canada. By Peter T. Rowley	48
Part II. Pathophysiology: Cellular and Molecular	
Current Perspectives on the Kinetics of Hemoglobin S Gelation. By PIER LUIGI SAN BIAGIO, JAMES HOFRICHTER, ANDREA MOZZARELLI, ERIC R. HENRY, and WILLIAM A. EATON	53
Kinetic Models and the Pathophysiology of Sickle Cell Disease. By Frank A. Ferrone	63
Intracellular Polymerization: Disease Severity and Therapeutic Predictions. By CONSTANCE TOM NOGUCHI, GRIFFIN P. RODGERS, and ALAN N. SCHECHTER	75
Pathology of Membrane Proteins in Sickle Erythrocytes. By ORAH S. PLATT	8:
Lipid Alterations and Cellular Properties of Sickle Red Cells. By BERTRAM LUBIN, FRANS KUYPERS, and DANIEL CHIU	80
Ion Content and Transport and the Regulation of Volume in Sickle Cells. By CARLO BRUGNARA, H. FRANKLIN BUNN, and DANIEL C. TOSTESON	96

<sup>&</sup>lt;sup>a</sup>This volume is the result of a conference entitled Sickle Cell Disease—Current Perspectives held from April 11 to April 13, 1988 in Bethesda, Md., cosponsored by the National Association for Sickle Cell Disease, Inc. and The New York Academy of Sciences.

## Part III. Clinical Aspects of Sickle Cell Disease

The Natural History of Sickle Cell Disease. By JEANNE A. SMITH	104
Geography and the Clinical Picture of Sickle Cell Disease: An Overview. By G. R. Serjeant	109
The Kidney, Hepatobiliary System, and Spleen in Sickle Cell Anemia. By HOWARD A. PEARSON	120
A Profile of Sickle Cell Disease in Nigeria. By OLUFEMI O. AKINYANJU	126
Delayed Growth and Sexual Maturation in Sickle Cell Disease. By Doris L. Wethers	137
Saudi Arabian Sickle Cell Anemia: A Molecular Approach. By Barbara A. Miller, Mohammed Salameh, Mohammed Ahmed, Nancy Olivieri, Titus H. J. Huisman, Stuart H. Orkin, and David G. Nathan	143
Part IV. Psychosocial Dimensions	
Do Pregnant Women Benefit from Hemoglobinopathy Carrier Detection? By Peter T. Rowley, Star Loader, C. J. Sutera, and Margaret Walden	152
The Impact of a Child with Sickle Cell Disease on Family Dynamics. By A. KATHLEEN BURLEW, ROBERT EVANS, and CARLTON OLER	161
Adjustment and Coping in Adolescents with Sickle Cell Disease. By ANITA LANDAU HURTIG and KWANG B. PARK	172
Family Structure and Intervention Strategies: Beyond Empirical Research. By PEGGYE DILWORTH-ANDERSON	183
Pain Management in Sickle Cell Disease: Rationale and Techniques. By RICHARD PAYNE	189
Part V. Clinical Modifiers of Sickle Cell Disease	
The Possible Role of Genetic Modifiers in the Clinical Severity of Sickle Cell Syndromes. By SERGIO PIOMELLI	207
Design and Testing of Antisickling Therapy. By SAMUEL CHARACHE	211
Alpha Thalassemia: A Modifier of Sickle Cell Disease. By STEPHEN H.  EMBURY	213
Chemotherapy and Hemoglobin F Synthesis in Sickle Cell Disease. By GEORGE J. DOVER and SAMUEL CHARACHE	222
Known and Potential Sources for Epistatic Effects in Sickle Cell Anemia. By RONALD L. NAGEL, MARY E. FABRY, DHANANJAYA K. KAUL, HENNY BILLETT, HELENA CROIZAT, DOMINIQUE LABIE, and MITZY CANESSA	228
Covalent Chemical Modifiers of Sickle Cell Hemoglobin. By HIROSHI UENO, YASUO BAI, and JAMES M. MANNING	239
Membrane Modifiers in Sickle Cell Disease. By LENNETTE J. BENJAMIN	247
The Influence of Fetal Hemoglobin on the Clinical Expression of Sickle Cell Anemia, By D. R. POWARS, L. CHAN, and W. A. SCHROEDER	262

Part VI. Hemorheology and Microcirculation in Sickle Cell Diseases
The Rheology of Sickle Cell Hemoglobin. By ROBIN W. BRIEHL
Mean Corpuscular Hemoglobin Concentration and Cell Deformability. By MARGARET R. CLARK
Hemoglobin S Polymerization: Fiber Lengths, Rheology, and Pathogenesis. By ROBIN W. BRIEHL and ERIC S. MANN
Role of Leukocyte-Endothelium Adhesion in Affecting Recovery from Ischemic Episodes. By HERBERT H. LIPOWSKY and SHU CHIEN
Erythrocytic and Vascular Factors Influencing the Microcirculatory Behavior of Blood in Sickle Cell Anemia. By D. K. KAUL, M. E. FABRY, and R. L. NAGEL
Rheological and Adherence Properties of Sickle Cells: Potential Contribution to Hematologic Manifestations of the Disease. By Narla Mohandas and Evan Evans
Hemodynamic Studies in Sickle Cell Disease. By GRIFFIN P. RODGERS, CONSTANCE TOM NOGUCHI, and ALAN N. SCHECHTER
Poster Papers
Adaptation and Coping of a Population of Sickle Cell Anemia Patients over 30 Years of Age. By M. R. ABRAMS, E. WHITWORTH, G. PHILLIPS, and K. NASH
Nonreductive Modification of Proteins by Glyceraldehyde. By A. SEETHARAMA ACHARYA, YOUNGNAN J. CHO, and BHUVANESHWARI DORAL
<ol> <li>6-Di (isobutyrylamino) hexanoic Acid as a Potential Therapeutic Agent for the Treatment of Sickle Cell Disease. By C. T. ACQUAYE, T. L. CARTER, T. T. MORSON, M. ZAHOOR, R. JOHNSON, H. MIZUKAMI, and C. BUSTAMANTE</li> </ol>
Polymerization of Partially Liganded Hemoglobin S. By K. ADACHI, J. KIM, and N. SHIBAYAMA
Noninvasive Detection of Cerebral Vasculopathy Using Transcranial Doppler and Magnetic Resonance Imaging. By Robert J. Adams, Fenwick T. Nichols, Taher El Gammal, Virgil McKie, Paul Milner, Kathy McKie, and Asma Fischer
Modification of the Intraerythrocytic Hemoglobin S Affinity for Oxygen by a Zinc Chelator. By A. I. ALAYASH, R. CASHON, and J. BONAVENTURA
Rheological Properties of Sickle Erythrocytes in the Steady State Predict the Frequency and Severity of the Sickle Cell Painful Crisis. By SAMIR K. BALLAS, JAMES LARNER, EUGENE D. SMITH, SAUL SURREY, ELIAS SCHWARTZ, and ERIC F. RAPPAPORT
The Effect of Alpha Thalassemia on the Clinical Course of Hemoglobin SC Disease. By Carol A. Talacki, James Larner, Elias Schwartz, Saul Surrey, Eric F. Rappaport, and Samir K. Ballas
Blood Center Initiatives and Role in Sickle Cell Disease. By KATHRYN M. BEATTIE and A. WILLIAM SHAFER

Health Care Adherence of Persons with Sickle Cell Disease: The Role of Social Support. By FAYE Z. BELGRAVE and SERINA K. GILBERT	369
Volume Regulation of Sickle Cells. By Yves Beuzard, Martine Levent, Lucie Mariani, Dora Bachir, Claude Prehu, Marie Dominique Rhoda, Frederic Galacteros, Dominique Vitoux, and Abdel Kraiem	371
Relation of the Peripheral Percent Fetal Hemoglobin Level and Burst-Promoting Activity Production to the Regulation of the Circulating Erythroid Progenitor Cell Population in Sickle Cell Anemia. By H. CROIZAT and R. L. NAGEL	373
Newborn Screening for Hemoglobinopathies: Facilitation by a TASCS Force.  By JAMES R. ECKMAN, THOMAS R. KINNEY, and MARY S. HARRIS	376
Experience with an Animal Model for Sickle Cell Vasoocclusion. By M. E. FABRY, R. L. NAGEL, and D. K. KAUL	379
α-Thalassemia among Pediatric Hemoglobin S Homozygotes: Molecular and Clinical Studies. By A. E. FELICE, J. ZHAO, A. KUTLAR, M. RHODES, K. MCKIE, and V. MCKIE	381
Hospital Length of Stay for Patients with Sickle Cell Disease: Implications under the Prospective Payment Plan. By SERINA K. GILBERT, FAYE Z. BELGRAVE, CHARLES HARRIS, and ROLAND B. SCOTT	383
Genetic Determinant for Increased Fetal Hemoglobin Linked to the Benin Haplotype in Some Sickle Cell Anemia Patients. By JOHN G. GILMAN and PAUL F. MILNER	385
Independent Origin of a $\beta^{S}$ -Globin Gene in a Caucasian with Sickle Cell Anemia. By Joseph E. Gootenberg, Corinne D. Военм, and HAIG H. KAZAZIAN, JR.	389
Nature of Cardiac Findings in Sickle Cell Anemia. By L. JULIAN HAYWOOD, CHERYL MARTIN, DOROTHY TATTER, SHARON NORRIS, and CAGE S. JOHNSON	393
Oxygen Promotes Sickling of SS Cells. By KAZUMI HORIUCHI and TOSHIO ASAKURA	395
Clinical and Molecular Characterization of Thalassemia Intermedia and Thalassemia Major in American Blacks. By J. M. GONZALEZ-REDONDO, T. A. STOMING, F. KUTLAR, A. KUTLAR, and T. H. J. HUISMAN	398
Vitamin E in Sickle Cell Disease Patients. By S. K. Jain, J. D. Ross, C. IZUNDU, G. MASTERS, and N. NANCE	402
Inhibition of Deoxygenation-Induced Cation Fluxes in Sickle Cells by Stilbene Disulfonates: Relationship between Deoxygenation and Drug Exposure. By CLINTON H. JOINER	404
Sickle Cell Trait as an Age-Dependent Risk Factor for Sudden Death in Basic Training. By JOHN A. KARK, SAMUEL K. MARTIN, JAMES J. CANIK, and CECIL U. HICKS	407
Electron Microscopic Quantitation of Hemoglobin S Polymer in SS Red Blood Cells and Rheological Correlation. By A. ANNE KAPERONIS, ROBERT G. KING, JEANNE A. SMITH, and SHIJ CHIEN	409

Modification of Oxygen Affinity in Sickle Cell Anemia. By C. S. Johnson, A. J. Keidan, M. C. Sowter, R. D. White, and J. Stuart	413
Influence of Amidation of Glu 43(β) on the Polymerization of Deoxy Hemoglobin S. By Lakshmi Khandke and A. Seetharama Acharya	416
Morphometry and Flow Dynamics of Conjunctival Microcirculation in Sickle Cell Disease. By J. Kurantsin-Mills, S. B. Cohen, G. Kaplan, P. Van Houten, L. S. Lessin, M. F. Rabb, and M. F. Goldberg	418
The Flow of Sickle Red Cells through Microvascular Bifurcations. By JOSEPH KURANTSIN-MILLS and LAWRENCE S. LESSIN	422
Haemophilus influenzae B Immunization of Children with Sickle Cell Diseases. By A. L. Frank, R. J. Labotka, S. Rao, L. R. Frisone, P. H. McVerry, J. S. Samuelson, H. S. Maurer, and R. Yogev	425
Steady State Ion and Flux Parameters of Sickling Deer Red Blood Cells. By P. K. LAUF, K. WILKIE, J. STEFKO, and N. C. ADRAGNA	428
Protein C Levels in Sickle Cell Diseases. By RAJ TERKONDA, SCOT EBBINGHAUS, T. LEE WILLOUGHBY, MARJORIE SIRRIDGE, REANER SHANNON, and ALAN LICHTIN	430
Rare Blood for Patients with Sickle Cell Anemia. By Delores Mallory, DOROTHY MALAMUT, and ANTHONY GINTHER	432
Molecular Genetic Approach to Newborn Screening for Sickle Cell Disease. By DAVID C. JINKS, MINDY VANDERFORD, J. FIELDING HEJTMANCIK, and EDWARD R. B. MCCABE	434
Is Chronic Transfusion Necessary to Prevent Recurrent Stroke in Children with Sickle Cell Disease? By SCOTT T. MILLER, SREEDHAR P. RAO, DIANE JENSEN, and AUDREY K. BROWN	435
Observation of Intracellular Sickle Cell Hemoglobin Polymers with a Differential Polarization Microscope. By H. MIZUKAMI, D. A. BEACH, C. BUSTAMANTE, and C. T. ACQUAYE	438
Modulation of the Yield Stress of Sickle and Normal Blood by Fibrinogen. By C. L. Morris and D. L. Rucknagel	440
Prevalence of Certain Clinically Significant Alloantibodies in Sickle Cell Disease Patients. By Ethel Patten, Sarala N. Patel, Bonnie Soto, and Rosalyn A. Gayle	443
Transfusion Management of Patients with Sickle Cell Disease. By ETHEL PATTEN, SARALA N. PATEL, BONNIE SOTO, and ROSALYN A. GAYLE	446
Erythroctye Membrane Protein Kinase C in Sickle Cell Disease. By M. RAMACHANDRAN, K. MCKIE, and E. C. ABRAHAM	449
Bone Scintigraphy in Patients with Sickle Cell Disease and Osteomyelitis. By SREEDHAR RAO, ARNOLD STRASHUN, and SCOTT MILLER	452
Hemorheologic Parameters in Children with Homozygous Sickle Cell Anemia Receiving Chronic Red Cell Transfusions for Large Cerebral Vessel Vasculopathy. By H. Sabio, V. McKie, K. McKie, T. L. Jeraldo, R. A. Adams, and A. E. Felice	455
Semisynthetic Approach for Site-Specific Mutations in the α-Chain of Hemoglobin S. By GIRISH SAHNI and A. SEETHARAMA ACHARYA	458

>

Transfusional Iron Overload in Sickle Cell Anemia: Relationship between Liver Iron, Magnetic Resonance Imaging Findings, and Hepatic Fibrosis. By SHARADA A. SARNAIK, CHUNG-HO CHANG, and RAMIRO HERNANDEZ	460
Effect of Sickle Cell Shape on Filterability. By EMILY ANN SCHMALZER	463
Rheological Action of Oxpentifylline and Structurally Related Xanthine Derivatives on Sickle Cells. By J. STUART, P. C. W. STONE, M. PLAYER, and Y. Y. BILTO	466
Initial Flow-Rate Filtration of Sickle Cells Correlates with Their Polymerization Tendency at Arterial Oxygen Tension. By J. STUART, M. A. GREEN, C. T. NOGUCHI, A. J. KEIDAN, and S. S. MARWAH	469
Micronutrient Status in Adult Patients with Sickle Cell Disease. By C. C. TANGNEY, G. PHILLIPS, R. A. BELL, P. FERNANDES, P. THOMAS, E. SEGERS, and S-M. WU	472
Index of Contributors	475

